

## Vitiligo, hypothyroidism and cardiomyopathy

**Yashdeep Gupta, Ariachery C. Ammini**

Department of Endocrinology, All India Institute of Medical Sciences, New Delhi, India

### ABSTRACT

Vitiligo in association with autoimmune endocrine disorders, especially with hypothyroidism, is not uncommon. Some amount of pericardial effusion is usually present in long-standing/untreated hypothyroidism. Here we describe the case of young male with, long-standing progressive vitiligo, presenting with congestive cardiac failure due to dilated cardiomyopathy and primary hypothyroidism. Cardiac dysfunction progressively improved with thyroid hormone replacement over a period of 2 years.

**Key words:** Hypothyroidism, cardiomyopathy, vitiligo

### INTRODUCTION

Vitiligo is a common skin disease characterized by the presence of hypopigmented lesions resulting from a reduction in the number and function of melanocytes.<sup>[1]</sup> Vitiligo has been described both in hyperthyroidism and hypothyroidism. Prevalence of vitiligo among patients with hypothyroidism is significantly higher compared with general population.<sup>[2]</sup> Although rare, cardiomyopathy has been described in patients with hypothyroidism. It is infrequently seen in this era due to widespread availability and a low threshold of doing thyroid function tests in case of suspicion of thyroid related symptoms or coexistent associations. To the best of our literature review, the association between the two in the background of long-standing vitiligo has not been previously described. Here we report long-term follow-up of a case of a young man with extensive early-onset vitiligo, congestive cardiac failure, and primary hypothyroidism.

### CASE REPORT

Mr A, 30 years, was admitted in May 2009 with complaints

of breathlessness (NYHA functional class III), easy fatigability, and weight gain, slowly progressive over a course of 5 years. He was never evaluated for his symptoms prior to this hospitalization. There was no history of chest pain, palpitations, smoking, hypertension, or diabetes mellitus. Medical history revealed that vitiligo was diagnosed when he was 6 years of age, for which he received intermittent treatment (oral psoralens) from 14 years of age. It was stopped completely 6 years back as his vitiligo was progressively increasing [Figure 1] and was not responding to treatment.

His physical examination revealed regular pulse rate of 60 per minute, blood pressure of 90/60 mm Hg, and respiratory rate of 32/min. His jugular venous pressure was raised, pedal edema was present along with crackles at lung bases, the liver was not enlarged, and there was no ascites on clinical examination. There was no goitre. His height was 157 cm and weight 43 kg (mid parental height 160 cm). Chest X-ray revealed cardiomegaly [Figure 2a] and ECG had sinus rhythm. An echocardiogram revealed global hypokinesia with left ventricular ejection fraction of 15–20% with mild mitral regurgitation, enlarged left atrium and ventricle, and mild pericardial effusion without any regional wall motion abnormality or any valvular abnormality. Ultrasound abdomen was normal.

Investigations at initial hospitalization revealed mildly elevated bilirubin (1.7 mg%) and deranged renal parameters (urea 49 mg%, serum creatinine of 2 mg%). Serum electrolytes, hemogram, blood glucose and aminotransferase

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**Corresponding Author:** Prof. A. C. Ammini, Department of Endocrinology and Metabolism, All India Institute of Medical Sciences, Ansari Nagar, New Delhi – 110 029, India. E-mail: aca433@yahoo.com

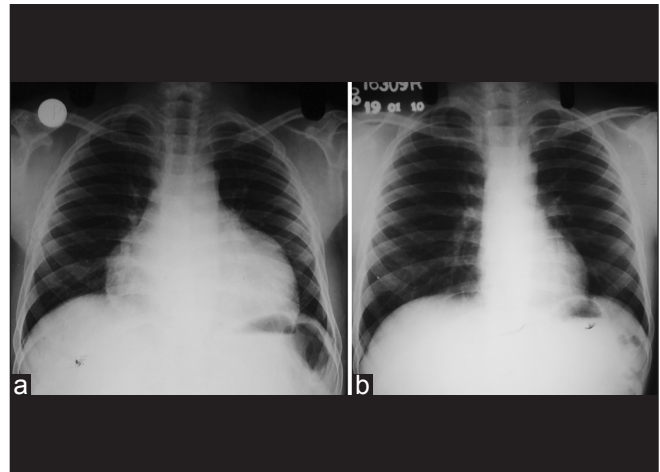


**Figure 1:** Posterior aspect of patient revealing extensive vitiligo

levels were normal. TSH was elevated (613 mIU/L), and free  $T_4$  0.17 ng/dl (normal 0.89–1.7 ng/dl) and free  $T_3$  0.51 pg/ml (normal 2.3–4.2 pg/ml) were low. Anti-TPO levels were 68.4 IU/ml (normal below 34 IU/ml). He was started on thyroxine (25  $\mu$ g escalated to 50  $\mu$ g) in addition to inotropes and diuretics (lasilactone once daily). In view of hypotension, vitiligo, severe hypothyroidism, and inappropriate cortisol response to stress (cortisol was 13.4  $\mu$ g/dl), he was also started on prednisolone (5 mg morning and 5 mg evening) which was tapered off after 2 weeks to 2.5 mg daily, continued till 3 months, and stopped with recovery of hypothalamic pituitary adrenal axis (cortisol 12.33  $\mu$ g/dl). His plasma testosterone was 4.52 ng/ml, luteinizing hormone 4.68 mIU/ml, follicle-stimulating hormone 6.75 mIU/ml, parathyroid hormone 50.98 pg/ml, and tissue transglutaminase 2.99 U/ml (negative). Patient symptoms pertaining to dyspnea were relieved after 2 weeks. His chest X-ray at follow-up after 8 months showed resolution of cardiomegaly [Figure 2b] {pretreatment cardiothoracic ratio: 60%, posttreatment cardiothoracic ratio: 44%}. The echocardiogram done at 1-year follow-up showed improvement in ejection fraction to 25–30%, with resolution of pericardial effusion. The left ventricular ejection fraction further improved to 45% at follow-up echocardiogram at 2 years. He was on carvedilol (3.125 mg twice daily) and thyroxine (50  $\mu$ g daily) on last follow-up (2 years). His TSH at last follow-up was 5.22  $\mu$ IU/ml (normal 0.27–4.2  $\mu$ IU/ml) and total thyroxine (total  $T_4$ ) was 9.5  $\mu$ g/dl (normal 5.1–14.1  $\mu$ g/dl).

## DISCUSSION

Vitiligo is an acquired depigmentation disorder that affects 0.5–2% of the general population.<sup>[3]</sup> It has frequent associations with several autoimmune diseases such as



**Figure 2:** (a) Chest X-ray PA view showing cardiomegaly before treatment. (b) Chest X-ray PA view showing resolution of cardiac enlargement after thyroxine supplementation at follow-up (8 months)

autoimmune thyroid disease (present in 14–34% of vitiligo patients).<sup>[4]</sup> Vitiligo can be present in all types of autoimmune polyglandular syndromes (APS), but the most frequent association appears to be in APS-3 which is defined as the association between autoimmune thyroiditis and another autoimmune disease. Hamburg, in his study of 321 patients of vitiligo, found hypothyroidism in 3.4% of the patients and laid emphasis on annual screening of thyroid functions in vitiligo patients.<sup>[3]</sup> Recent study from India in 50 subjects of vitiligo has found high prevalence of subclinical hypothyroidism (32%).<sup>[5]</sup> Vitiligo precedes thyroid dysfunction by many years giving an opportunity to screen these high-risk individuals before development of thyroid disease. A missed opportunity can result in severe comorbidity as is highlighted in our case.

Hypothyroid state may induce several cardiac manifestations including pericardial effusion and cardiac muscle impairment. Although cardiac output is reduced in hypothyroidism, heart failure is relatively rare because of low demand for peripheral oxygen delivery. Further, the symptoms associated with hypothyroidism such as fatigue, weight gain, and dyspnea on exertion are also the primary symptoms of heart failure, and this overlap obscures the clinical suspicion for thyroid assessment.

Dilated cardiomyopathy as a disease entity has a poor prognosis in itself due to progressive and irreversible myocardial dysfunction, barring the situation in which a metabolic cause is identified and specific therapy is instituted early. Several mechanisms have been proposed for hypothyroidism-induced myocardial injury, such as reduce muscle energy production, which may result in extensive muscle cell injury when muscle energy production falls below demand.<sup>[6,7]</sup> Another possible mechanism is related

to increased oxidative stress, due to reduced glutathione levels in the myocardial tissue causing direct myocardial damage<sup>[8]</sup> and third possible mechanism is reduction of sarcoplasmic/endoplasmic reticulum  $Ca^{2+}$ -ATPase and  $\alpha$ -myosin heavy chain in the hypothyroid heart, which may cause systolic and diastolic dysfunction.<sup>[9]</sup> Despite these proposed mechanisms, the exact mechanism of hypothyroidism induced myocardial injury is unknown. The reversibility of these changes after thyroxine treatment is unknown, and in long-term hypothyroid state, irreversible myocardial damage may occur and complete reversibility of cardiac status may not occur even after correction of thyroid status.<sup>[10]</sup> The early diagnosis of the disease state and institution of specific therapy may prevent irreparable damage.

Our case shows that hypothyroidism can produce the picture of a primary congestive cardiomyopathy and that thyroxine replacement therapy can alleviate the symptoms of patient and can result in improvement in structural and functional status of cardiovascular system. This case also highlights the association of thyroid disease with childhood onset vitiligo. We stress upon screening of thyroid status by TSH in heart failure (class 1 recommendation for initial evaluation of heart failure patients as per the heart failure guidelines)<sup>[11]</sup> and in patients with vitiligo, once per year, as suggested by Hamburg study<sup>[3]</sup> and Uncu *et al.*<sup>[12]</sup>

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